

## **REMARKS**

### **Status of the Claims**

Claims 22, 24-29, and 31-39 are pending and under examination. This paper makes no claim amendments or cancellations.

### **Rejection Under 35 U.S.C. § 103**

All examined claims remain rejected as obvious over Roth et al. (U.S. Patent 5,747,469) in view of either or both of Lu et al. (Cancer Res. 62: 1305-1310, 2002) or Tango et al. (Hum. Gene Ther. 13: 1373-1382, 2002), Almond et al. (WO 99/47690), and Tiemann (WO 01/11063).

Applicant respectfully traverses this rejection and submits that the Examiner has failed to establish a *prima facie* case of obviousness for reasons already made of record. The Examiner's attention is directed to the arguments made in Applicant's Response of August 13, 2007.

Notwithstanding Applicant's traversal of the *prima facie* case, Applicant takes this opportunity to present new and remarkable data demonstrating that the use of a single promoter bicistronic vector yield unexpectedly better results for treating p53-positive cancer cells than what is predicted by the prior art's simultaneous use of individual vectors.

In the accompanying Declaration by Dr. Ruth Gjerset under 37 C.F.R. § 1.132, Dr. Gjerset describes the results of recent experiments directly comparing the effect on p53-positive cancer cells of a single promoter bicistronic vector encoding p53 and p14ARF to the combined use of two vectors encoding the genes individually.

In the Declaration, Dr. Gjerset attests that the results predicted from the use of a single promoter bicistronic construct are approximately comparable to those that would be obtained using the two genes individually. However, despite predictions of approximate comparability, Dr. Gjerset demonstrates that the single promoter bicistronic vector is about 40-fold more effective for treating p53-positive cancer cells compared to the individual vectors used in

combination. This result is surprising and unexpected in view of the prior art expectation of relative comparability.

In sum, Applicants clearly demonstrate unexpected and superior results in the treatment of cancer cells using of a bicistronic construct comprising p53 and p14ARF, wherein both coding sequences were under the control of a single promoter. Accordingly, even if a *prima facie* case of obviousness has been made (which it has not), the rejection is traversed by the unexpected results provided in the specification. For the foregoing reasons, Applicants submit that the presently claimed invention is unobvious and that this rejection should be withdrawn.

### CONCLUSION

Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741

Respectfully submitted,

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Enclosures—Bressac et al. (*Proc. Natl. Acad. Sci. USA*, Vol. 87, 1973-1977, March 1990)  
Huang et al. (*Cancer Research*, Vol. 63, 3646-3653, July 1, 2003)